REMARKS

Claims 1-106 are pending in the instant application. New Claims 107-113 have been added by the present amendment. No new matter has been added.

NEW CLAIMS

Applicants have added new Claims 107-113 by the present amendment. New Claim 107 recites a method of treating a culture for bovine viral diarrhea virus (BVDV) infection, comprising administering to the culture a compound selected from the group consisting of Formula (I)-Formula (VI) in an amount sufficient to treat the BVDV infection. New Claim 108 recites the method of new Claim 107, wherein the culture is selected from one of a cell culture and a tissue culture. Support for new Claim 107 and new Claim 108 can be found on page 3, paragraph 0014; page 14, paragraph 0070; and in Examples 13, 15, and 24 of the application as filed.

More particularly, page 3, paragraph 0014, of the application as filed suggests adding an anti-viral agent to a culture medium. Page 14, paragraph 0070 suggests adding an active compound to a medium in which an embryo is being obtained. Further, Example 13, on pages 27-28 of the application as filed, provides a method for screening antiviral compounds for anti-BVDV activity. This method further discloses a method of treating cells inoculated with BVDV in a medium containing test antiviral compounds. See page 27, paragraph 00153 of the application as filed. This method also discloses a method of adding a solution comprising an antiviral compound to the cell medium. See page 28, paragraph 00154 of the application as filed. Additional support for new Claim 107 and new Claim 108 can be found in Example 15 of the application as filed. More particularly, Example 15, on page 29 of the application as filed discloses a method of preparing tissue culture passages of samples infected with BVDV to optimize isolation of BVDV. See page 29, paragraph 00162 of the application as filed. Additionally, Example 24, pages 34-35, of the application as filed provides experimental data related to the analysis of in vitro culture media and cell lysates that have been treated with an antiviral compound after exposure to BVDV.

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New Claim 109 recites a method of treating an embryo for bovine viral diarrhea virus (BVDV) infection, comprising administering to the embryo a compound selected from the group consisting of Formula (I)-Formula (VI) in an amount sufficient to treat the BVDV infection. New Claim 110 recites the method of new Claim 109, wherein the embryo comprises an *in vitro*-produced embryo. Support for new Claim 109 and new Claim 110 can be found in Claims 57 and 63 of the application as filed. Claim 57, which is ultimately dependent from Claim 53, recites a method of treating BVDV infection in a subject in need of such treatment, comprising administering to the subject a compound selected from the group consisting of Formula I and Formula II, wherein the subject is an embryo. Likewise, Claim 63, which is ultimately dependent from Claim 61, recites a method of treating BVDV infection in a subject in need of such treatment, comprising administering to the subject a compound selected from the group consisting of Formula V and Formula VI, wherein the subject is an embryo.

Further support for new Claim 109 and new Claim 110 can be found in paragraph 0013 on page 2 of the application as filed. More particularly, paragraph 0013 discusses the problem wherein *in vitro*-produced bovine embryos can be potential vectors for transmission of BVDV, thereby introducing BVDV into the embryo production system and resulting in contaminated *in vitro* fertilized embryos or cell lines. See page 2, paragraph 0013. Additional support for new Claim 109 and new Claim 110 can be found on page 13, paragraph 0068, of the application as filed, which describes one embodiment of the disclosed subject matter, wherein the subject is a live embryo, which can be *in utero* or *in vitro* (in the case of an embryo being maintained for *in vitro* fertilization).

New Claim 111 recites a method of treating bovine viral diarrhea virus (BVDV) in a culture medium surrounding an *in vitro*-produced embryo, comprising administering to the culture medium a compound selected from the group consisting of Formula (I)-Formula (VI) in an amount sufficient to treat the BVDV. Support for new Claim 111 can be found on page 3, paragraph 0014, of the application as filed, which suggests adding an anti-viral agent to the culture medium surrounding *in vitro*-produced embryos to prevent or reduce transmission of virus to the embryo or embryo recipient. Additional support for new Claim 111 can be found in Example 24, pages 34-35, of the application

as filed, which describes the treatment of *in vitro* culture media with antiviral compounds of the instant application. The corresponding results are provided in Tables 2-5 and accompanying text.

New Claim 112 recites a method of preparing a biological specimen or medium for use in an *in vitro* fertilization procedure, the method comprising:

- (a) providing the biological specimen or medium; and
- (b) administering to the biological specimen or medium a compound selected from the group consisting of Formula (I)-Formula (VI) in an amount sufficient to treat the biological specimen or medium for a BVDV infection.

New Claim 113 recites the method of new Claim 113, wherein the biological specimen or medium comprises a gamete, a serum, a somatic cell, an oocyte, a cumulus oocyte complex (COC), an embryo, a culture medium surrounding an embryo, and combinations thereof.

Support for new Claim 112 can be found in Examples 17-23, which provide a method of preparing biological specimens and media for use in an *in vitro* fertilization procedure. See Examples 17-23, pages 30-34, of the application as filed. In particular, Examples 17-19 provide a method of exposing the mature oocytes, or cumulus oocyte complexes (COCs) to BVDV. See pages 30-32 of the application as filed. Further, Examples 20 and 21 provide a method of *in vitro* fertilization of the BVDV-infected COCs with bovine semen and separated spermatozoa and subsequent *in vitro* development of the infected embryos. See page 32, paragraphs 00182-00187, of the application as filed. Examples 22 and 23 provide methods for the further preparation of the infected embryos and subsequent assay of the samples for BVDV. See Examples 22 and 23, pages 32-33 of the application as filed. The treatment of the *in vitro* culture media and cell lystates with antiviral compounds of the instant application and corresponding results are provided in Tables 2-5 and accompanying text. See Example 24, pages 34-35 of the application as filed.

Additional support for new Claim 112 and new Claim 113 can be found on page 3, paragraph 0014, which suggests the addition of an antiviral agent to *in vitro* embryo production systems to prevent or reduce transmission of BVDV to the embryo or embryo recipient. Additional support for new Claim 113 can be found on page 2,

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paragraph 0013, which provides that BVDV can be introduced into the embryo production system in association with gametes, such as spermatozoa and oocytes, serum, somatic cells, and cumulus oocyte complexes (COCs), which can result in contaminated *in vitro* fertilized (IVF) embryos or cell lines.

Further support for new Claim 112 and new Claim 113 can be found on page 13, paragraph 0068, of the application as filed, which describes one embodiment of the presently disclosed subject matter, wherein the subject is a live embryo, which can be *in utero* or *in vitro* (in the case of an embryo being maintained for *in vitro* fertilization). Additional support for new Claim 112 and new Claim 113 can be found on page 14, paragraph 0070, which describes an embodiment of the presently disclosed subject matter wherein the treatment is carried out during an *in vitro* fertilization procedure, wherein the compounds can be administered to the embryo by adding the active compound, in a suitable concentration, to the medium in which the embryo is being obtained.

Applicants submit that new Claims 107-113 are now in condition for allowance and respectfully request formal allowance of Claims 107-113. No new matter has been added.

DEPOSIT ACCOUNT

The Commissioner is hereby authorized to charge any fees associated with the filing of this correspondence to Deposit Account No. <u>50-0426</u>.

By:

Respectfully submitted,

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